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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,432	11/10/2003	Wojtek Auerbach	REG 784	4884
26693	7590	10/10/2008	EXAMINER	
REGENERON PHARMACEUTICALS, INC			MONTANARI, DAVID A	
777 OLD SAW MILL RIVER ROAD				
TARRYTOWN, NY 10591			ART UNIT	PAPER NUMBER
			1632	
			MAIL DATE	DELIVERY MODE
			10/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)
	10/705,432	AUERBACH ET AL.
	Examiner	Art Unit
	David Montanari	1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 August 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) The period for reply expires _____ months from the mailing date of the final rejection.
- b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because

- (a) They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) They raise the issue of new matter (see NOTE below);
- (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. Applicant's reply has overcome the following rejection(s): _____.

6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. For purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: NONE.

Claim(s) objected to: NONE.

Claim(s) rejected: 25-28.

Claim(s) withdrawn from consideration: NONE.

AFFIDAVIT OR OTHER EVIDENCE

8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.

12. Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____

13. Other: _____.

/Peter Paras, Jr./
Supervisory Patent Examiner, Art Unit 1632

Continuation of 11. does NOT place the application in condition for allowance because: Applicant's arguments and amendments to the pending claims are not found persuasive. Applicants argue in amendment filed on 8/12/2008 that they have amended claim 25 to include the subject matter that the Examiner deemed enabled and to refer to mouse ES cell colonies. Applicants continue to argue that claim 25 is also amended to indicate that the second targeting number is proportionately at least two-fold higher to reflect the practical aspects of screening known to those skilled in the art. These arguments are not persuasive.

Response to Arguments

On pg. 4 of the Final rejection mailed on 8/4/2008 (2nd, parag.) it was stated that the claimed invention does not increase targeting frequency of a targeting construct, but rather the claimed invention is drawn to a method of comparing two different promoters, PGK and ubiquitin (Final, 8/4/2008, pg. 4 parag. 3 lines 1-3). This is clearly reflected in working example 1 on pg. 10 of the specification which teaches that the ubiquitin promoter is better at driving expression of a drug resistance gene compared to a PGK promoter (pg. 10, parag. 0042 lines 1-3). As on pg. 6 of the Final rejection (8/4/2008) the scope rejection was written to reflect what Applicant has presented in their working example and Table 2, which is merely a comparison between two promoters and their ability to drive a drug resistance gene in mouse ES cells. This comparison between the ubiquitin and PGK promoters does not amount to or enable a method of increasing targeting frequency of a targeting construct in mouse ES cells, but rather demonstrates that one particular promoter is stronger with respect to transgene expression, which in this case is a drug resistance gene.

Further in the Non-Final rejection mailed on 11/1/2007 it was stated that "Applicant has contrasted two different promoters and attempted to use the data to further limit the claimed method" (pg. 4 lines 13-14) and that Applicants arguments stating unexpected results with the ubiquitin promoter are not persuasive since the art of record teaches that ubiquitin is one of the best promoters to use to drive gene expression (pg. 4 last 5 lines).

To summarize, nothing in steps a-f of claim 25 would result in a method of increasing targeting frequency of a targeting construct in mouse ES cells. The scope of enablement in the Final rejection mailed on 8/4/2008 made clear that the claimed invention is only a comparison between two different promoters and the claimed invention as well as the specification do not support or amount to a method of increasing targeting frequency when practicing steps a-f of claim 25.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID MONTANARI whose telephone number is (571)272-3108. The examiner can normally be reached on M-Tr 8-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 1-571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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AU 1632